IN THE SPECIFICATION

Please amend the specification as follows: .

Page 1, after the Title ("Chaperone Fragments") kindly insert:

--**RELATED APPLICATIONS**

This application is a continuation-in-part of PCT/GB97/02652, filed September 26, 1997, designating the U.S., claiming priority from PCT/GB96/02980, filed December 3, 1996 and GB 9620243.7, filed September 26, 1996; and, each of these documents, as well as all documents cited herein, and all documents referenced or cited in documents cited herein, are hereby incorporated herein by reference.

FIELD OF THE INVENTION--.

Page 1, between the first and second paragraphs (after "diagnostics." and before "Chaperones") please insert:

--**BACKGROUND OF THE INVENTION**--.

Page 7, between the first and second paragraphs (after "(<10% homology)." and before "The present inventors …") please insert:

--**OBJECTS AND SUMMARY OF THE INVENTION**--.

Page 7, third paragraph, please insert --a-- between "In" and "first".

Page 9, first paragraph, please insert --a-- between "In" and "second".

Page 9, ~~first~~ 2nd paragraph, please insert --a-- between "In" and "third".

Page 10, first full paragraph, please insert --a-- between "In" and "fourth".

Page 11, first full paragraph, please insert --a-- between "In" and "fifth".

Page 11, second full paragraph, please insert --a-- between "In" and "sixth".

Page 12, fourth paragraph, please insert --a-- between "In" and "seventh".

Page 13, third paragraph, please insert --an-- between "In" and "eighth" and please delete "as claimed in any preceding claim".

Page 14, before the first full paragraph (before "A preferred polypeptide ...") please insert:

--The term "...*et seq* ..." can have its ordinary meaning and thus the invention can include a polypeptide which comprises an amino acid sequence selected from GroEL residues between 228-273 and 194-328 such as: 227-273, 227-274, 226-274, 226-275, 225-275, 225-276, 224-276, 224-277, 223-277, 223-278, 222-278, 222-279, 221-279, 221-280, 220-280, 220-281, 219-281, 219-282, 218-282, 218-283, 217-283, 217-284, 216-284, 216-285, 215-285, 215-286, 214-286, 214-287, 213-287, 213-288, 212-288, 212-289, 211-289, 211-290, 210-290, 210-291, 209-291, 209-292, 208-292, 208-293, 207-293, 207-294, 206-294, 206-295, 205-295, 205-296, 204-296, 204-297, 203-297, 203-298, 202-298, 202-299, 201-299, 201-300, 200-300, 200-301, 199-301, 199-302, 198-302, 198-303, 197-303, 197-304, 196-304, 196-305, 195-305, 195-306, 194-306, 194-307, 195-328, 195-327, 196-327, 196-326, 197-326, 197-325, 198-325, 198-324, 199-324, 199-323, 200-323, 200-322, 201-321, 201-320, 202-320, 202-319, 203-319, 203-318, 204-318, 204-317, 205-317, 205-316, 206-316, 206-315, 207-315, 207-314, 208-314, 208-313, 209-313, 209-312, 210-312, 210-311, 211-311, 211-310, 212-310, 212-309, 213-309, 213-308, 214-308, 214-307, 215-307, 215-306, 216-306, 216-305, 217-305, 217-304, 218-304, 218-303, 219-303, 219-302, 220-302, 220-301, 221-301, 221-300, 222-300, 222-299, 223-299, 223-298, 224-298, 224-297, 225-297, 225-296, 226-296, 226-295, 227-295, 227-294, 221-303, 222-302, 223-301, 224-300, 225-299, 226-298, 227-297, 228-296, *inter alia*.--

Page 14, second to last line, and page 15, line 1, after "preferably" and before "75%" (each occurrence), please insert: --at least--.

Page 15, after line 3 ("residues.") and before line 4 ("The hsp60 class ..."), please insert:

--Of course, substantially homologous amino acid sequences and nucleotide sequences can have greater than 75% homology (e.g., at least 80% homology, or at least 85% homology, such as at least 90% homology, or even at least 95% homology ,for instance at least 97% homology). Nucleotide sequence homology can be determined using the "Align" program of Myers and Miller, ("Optimal Alignments in Linear Space", CABIOS *4*, 11-17, 1988, incorporated herein by reference) and available at NCBI. Alternatively or additionally, the term "homology", for instance, with respect to a nucleotide or amino acid sequence, can indicate a quantitative measure of homology between two sequences. The percent sequence homology can be calculated as $(N_{ref} - N_{dif})*100/N_{ref}$, wherein N_{dif} is the total number of non-identical residues in the two sequences when aligned and wherein N_{ref} is the number of residues in one of the sequences. Hence, the DNA sequence AGTCAGTC will have a sequence similarity of 75% with the sequence AATCAATC (N_{ref} = 8; N_{dif}=2). Alternatively or additionally, "homology" with respect to sequences can refer to the number of positions with identical nucleotides or amino acids divided by the number of nucleotides or amino acids in the shorter of the two sequences wherein alignment of the two sequences can be determined in accordance with the Wilbur and Lipman algorithm (Wilbur and Lipman, 1983 PNAS USA 80:726, incorporated herein by reference), for instance, using a window size of 20 nucleotides, a word length of 4 nucleotides, and a gap penalty of 4, and computer-assisted analysis and interpretation of the sequence data including alignment can be conveniently performed using commercially available programs (e.g., Intelligenetics ™ Suite, Intelligenetics Inc. CA).. When RNA sequences are said to be similar, or have a degree of sequence identity or homology with DNA sequences, thymidine (T) in the DNA sequence is considered equal to uracil (U) in the RNA sequence.

RNA sequences within the scope of the invention can be derived from DNA sequences, by thymidine (T) in the DNA sequence being considered equal to uracil (U) in RNA sequences.

Additionally or alternatively, amino acid sequence similarity or identity or homology can be determined using the BlastP program (Altschul *et al.*, Nucl. Acids Res. 25, 3389-3402, incorporated herein by reference) and available at NCBI.. The following references (each incorporated herein by reference) provide algorithms for comparing the relative identity or homology of amino acid residues of two proteins, and additionally or alternatively with respect to the foregoing, the teachings in these references can be used for determining percent homology or identity: Needleman SB and Wunsch CD, "A general method applicable to the search for similarities in the amino acid sequences of two proteins," J. Mol. Biol. 48:444-453 (1970); Smith TF and Waterman MS, "Comparison of Bio-sequences," Advances in Applied Mathematics 2:482-489 (1981); Smith TF, Waterman MS and Sadler JR, "Statistical characterization of nucleic acid sequence functional domains," Nucleic Acids Res., 11:2205-2220 (1983); Feng DF and Dolittle RF, "Progressive sequence alignment as a prerequisite to correct phylogenetic trees," J. of Molec. Evol., 25:351-360 (1987); Higgins DG and Sharp PM, "Fast and sensitive multiple sequence alignment on a microcomputer," CABIOS, 5: 151-153 (1989); Thompson JD, Higgins DG and Gibson TJ, "ClusterW: improving the sensitivity of progressive multiple sequence alignment through sequence weighing, positions-specific gap penalties and weight matrix choice, Nucleic Acid Res., 22:4673-480 (1994); and, Devereux J, Haeberlie P and Smithies O, "A comprehensive set of sequence analysis program for the VAX," Nucl. Acids Res., 12: 387-395 (1984).

Likewise, from the text herein, one skilled in the art can determine what is meant by "homology" and "substantially homologous" without any undue experimentation, such that these terms are clear and definite (note for instance the following text).--.

Page 22, first full paragraph, please change "The polypeptide" to --In a ninth aspect, the invention provides a polypeptide which--.

Page 24, third paragraph, please insert --a-- between "In" and "tenth".

Page 26, second full paragraph, please insert --an-- between "In" and "eleventh".

Page 26, third full paragraph, please insert --a--between "In" and "twelfth".

Page 26, last paragraph, please insert --a-- between "In" and "thirteenth".

Page 27, first full paragraph, please insert --a-- between "In" and "fourteenth".

Page 31, second full paragraph, please insert --a-- between "In" and "fifteenth".

Page 31, the paragraph spanning pages 31-32, please insert --a-- between "In" and "sixteenth".

Page 32, first full paragraph, please insert --a-- between "In" and "seventeenth".

Page 32, at the end of the second full paragraph (after "about 1:1") please insert --And, this can be an eighteenth aspect of the invention.--

Page 32, third full paragraph, please insert --a-- between "In" and "nineteenth".

Page 32, fourth full paragraph, please insert --a-- between "In" and "twentieth"--.

Page 32, last (fifth full) paragraph, please insert --a-- between "In" and "twenty-first".

Page 33, first full paragraph, please insert --a-- between "In" and "twenty-second".

Page 33, second full paragraph, please insert --a-- between "In" and "twenty-third".

Page 33, between the second and third full paragraphs (after "antagonist thereof" and before "The momomeric apical domain") please insert:

--A construct encoding a polypeptide of the invention or an antagonist thereof would be a vector or a recombinant for expression of the polypeptide or antagonist. The methods for making and/or administering a vector or recombinant for expression of such agents either *in vivo* or *in vitro* can be any desired method, e.g., a method which is by or analogous to the methods disclosed in: U.S. Patent Nos. 4,603,112, 4,769,330, 5,174,993, 5,505,941, 5,338,683, 5,494,807, 4,722,848, WO 94/16716, WO 96/39491, Paoletti, "Applications of pox virus vectors to vaccination: An update," PNAS USA 93:11349-11353, October 1996, Moss, "Genetically engineered poxviruses for recombinant gene expression, vaccination, and safety," PNAS USA 93:11341-11348, October 1996, Smith et al., U.S. Patent No. 4,745,051 (recombinant baculovirus), Richardson, C.D. (Editor), Methods in Molecular Biology 39, "Baculovirus Expression Protocols" (1995 Humana Press Inc.), Smith et al., "Production of Huma Beta Interferon in Insect Cells Infected with a Baculovirus Expression Vector," Molecular and Cellular Biology, Dec., 1983, Vol. 3, No. 12, p. 2156-2165; Pennock et al., "Strong and Regulated Expression of *Escherichia coli* B-Galactosidase in Infect Cells with a Baculovirus vector," Molecular and Cellular Biology Mar. 1984, Vol. 4, No. 3, p. 399-406; EPA 0 370 573, U.S. application Serial No. 920,197, filed October 16, 1986, EP Patent publication No. 265785, U.S. Patent No. 4,769,331 (recombinant herpesvirus), Roizman, "The function of herpes simplex virus genes: A primer for genetic engineering of novel vectors," PNAS USA 93:11307-11312, October 1996, Andreansky et al., "The application of genetically engineered herpes simplex viruses to the treatment of experimental brain tumors," PNAS USA 93:11313-11318, October 1996, Robertson et al. "Epstein-Barr virus vectors for gene delivery to B lymphocytes," PNAS USA 93:11334-11340, October 1996, Frolov et al., "Alphavirus-based expression vectors: Strategies and applications," PNAS USA 93:11371-11377, October 1996, Kitson et al., J. Virol.

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65, 3068-3075, 1991; U.S. Patent Nos. 5,591,439, 5,552,143 (recombinant adenovirus), Grunhaus et al., 1992, "Adenovirus as cloning vectors," Seminars in Virology (Vol. 3) p. 237-52, 1993, Ballay et al. EMBO Journal, vol. 4, p. 3861-65, Graham, Tibtech 8, 85-87, April, 1990, Prevec et al., J. Gen Virol. 70, 429-434, PCT WO91/11525, Felgner et al. (1994), J. Biol. Chem. 269, 2550-2561, Science, 259:1745-49, 1993 and McClements et al., "Immunization with DNA vaccines encoding glycoprotein D or glycoprotein B, alone or in combination, induces protective immunity in animal models of herpes simplex virus-2 disease," PNAS USA 93:11414-11420, October 1996, and U.S. Patents Nos 5,591,639, 5,589,466, and 5,580,859 relating to DNA expression vectors, *inter alia*. See also WO 98/33510; Ju et al., Diabetologia, 41:736-739, 1998 (lentiviral expression system); Sanford et al., U.S. Patent No. 4,945,050 (method for transporting substances into living cells and tissues and apparatus therefor); Fischbach et al. (Intracel), WO 90/01543 (method for the genetic expression of heterologous proteins by cells transfected); Robinson et al., seminars in IMMUNOLOGY, vol. 9, pp.271-283 (1997) (DNA vaccines); Szoka et al., U.S. Patent No. 4,394,448 (method of inserting DNA into living cells); and McCormick et al., U.S. Patent No. 5,677,178 (use of cytopathic viruses for therapy and prophylaxis of neoplasia).

The expression product generated by vectors or recombinants in this invention optionally can also be isolated and/or purified from infected or transfected cells; for instance, to prepare compositions for administration to patients. However, in certain instances, it may be advantageous to not isolate and/or purify an expression product from a cell; for instance, when the cell or portions thereof enhance the effect of the polypeptide or the antagonist thereof.

More generally, compositions for use in the invention, e.g., compositions containing antibodies or polypeptides or antagonists or vectors or recombinants, can be prepared in

accordance with standard techniques well known to those skilled in the pharmaceutical or medical arts. Such compositions can be administered in dosages and by techniques well known to those skilled in the medical arts taking into consideration such factors as the age, sex, weight, and condition of the particular patient, and the route of administration and the condition or disease being treated. The compositions can be administered alone, or can be co-administered or sequentially administered with other compositions of the invention or with other prophylactic or therapeutic compositions.

Examples of compositions of the invention include liquid preparations for orifice, e.g., oral, nasal, anal, genital (e.g., vaginal), vascular and/or SMC, etc., administration such as suspensions, syrups or elixirs; and, preparations for parenteral, subcutaneous, intradermal, intramuscular, intravenous, intraarterial, intralymphatic, or intraperitoneal administration (e.g., injectable administration) such as sterile suspensions or emulsions. In such compositions the active agent can be in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose or the like.

The compositions of the invention may be packaged in a single dosage form for immunization by parenteral (i.e., intramuscular, intradermal or subcutaneous) administration or orifice administration, e.g., perlingual (i.e., oral), intragastric, mucosal including intraoral, intraanal, intravaginal, intravenous, intralymphatic, intraarterial, intraperitoneal, and the like administration. Accordingly, compositions in forms for such administration routes are envisioned by the invention. And again, the effective dosage and route of administration are determined by known factors, such as age, sex, weight, condition and nature of patient disease or condition being treated, as well as LD_{50} and other screening procedures which are known and do not require undue experimentation.

Dosages of each active agent can range from a few to a few hundred micrograms, e.g., 5 to 500 μg. An inventive vector or recombinant expressing a polypeptide and/or an antagonist thereof can be administered in any suitable amount to achieve expression at these dosage levels. The inventive vector or recombinant can be administered to a patient or infected or transfected into cells in an amount of about at least 10^3 pfu; more preferably about 10^4 pfu to about 10^{10} pfu, e.g., about 10^5 pfu to about 10^9 pfu, for instance about 10^6 pfu to about 10^8 pfu. And, if more than one gene product is expressed by more than one recombinant, each recombinant can be administered in these amounts; or, each recombinant can be administered such that there is, in combination, a sum of recombinants comprising these amounts. Other suitable carriers or diluents can be water or a buffered saline, with or without a preservative. The expression product or isolated product or vector or recombinant may be lyophilized for resuspension at the time of administration or can be in solution. Antibodies can be humanized to enhance their effects. See, e.g., Huls et al., "A recombinant, fully human monoclonal antibody with antitumor activity constructed from phage-displayed antibody fragments," Nature Biotechnology Vol. 17, No. 3, March 1999, and documents cited therein, incorporated herein by reference.

In plasmid compositions, the dosage should be a sufficient amount of plasmid to elicit a response analogous to compositions wherein the agent or agents are directly present; or to have expression analogous to dosages in such compositions; or to have expression analogous to expression obtained *in vivo* by recombinant compositions. For instance, suitable quantities of plasmid DNA in plasmid compositions can be 1 *u*g to 100 mg, preferably 0.1 to 10 mg, e.g., 500 micrograms, but lower levels such as 0.1 to 2 mg or preferably 1-10 *u*g may be employed. Documents cited herein regarding DNA plasmid vectors may be consulted for the skilled artisan

to ascertain other suitable dosages for DNA plasmid vector compositions of the invention, without undue experimentation.

For treatment of a disease, the compositions comprising the polypeptide and/or the antagonist thereof, alone or with other treatment, may be administered as desired by the skilled medical practitioner, from this disclosure and knowledge in the art, e.g., at the first signs or symptoms, or as soon thereafter as desired by the skilled medical practitioner, without any undue experimentation required; and, the administration of the compositions, alone or with other treatment, may be continued as a regimen, e.g., monthly, bi-monthly, biannually, annually, or in some other regimen, by the skilled medical practitioner for such time as is necessary to prevent or treat the disease, without any undue experimentation required.

For prevention of a disease, the compositions, alone or with other treatment, may be administered at the first indication of the patient being prone to the disease, or as soon thereafter as desired by the skilled medical practitioner, in any desired regimen, such as a single administration or multiple administrations in a regimen as desired, e.g., monthly, bi-monthly, biannually, or any combination thereof, or in some other regimen, by the skilled medical practitioner for such time as is necessary to prevent the disease, without any undue experimentation required.--

Page 37, before the first line, please insert:

--**BRIEF DESCRIPTION OF THE DRAWINGS**--.

Page 39, after the fourth full paragraph (after line 8, actual count, i.e., after "for comparison.") and before "Example 1" (before line 9, actual count), please insert:\

--**DETAILED DESCRIPTION**

EXAMPLES--.